REMARKS

Claim 18 and 23 have been amended. Support for the amendment to Claim 18 can be found, for example, in canceled Claim 22. New Claims 38-51 have been added. Support for new Claims 38-51 can be found in the specification, for example, at paragraphs [0013], [0019], [0021], [0053], [0056], [0058], [0059], [0113]-[0116], [0123], and [0134]. Claims 1-17 are withdrawn from consideration. Accordingly, Claims 18-21 and 23-51 are presented for further consideration.

Rejections under 35 U.S.C. § 102(b)

Claims 18, 25, and 27

Claims 18, 25, and 27 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 4,240,751 to Linnecke and Wong (hereinafter "Linnecke").

Claim 18 has been amended to include the features of canceled Claim 22, which is not rejected under 35 U.S.C. § 102(b) as anticipated by Linnecke. At least for this reason, Applicants request withdrawal of the rejections of amended Claim 18 and Claims 25 and 27, which depend from Claim 18, under 35 U.S.C. § 102(b).

Rejections under 35 U.S.C. § 103(a)

It is well settled that the Examiner "bears the initial burden of presenting a *prima facie* case of unpatentability..." *In re Sullivan*, 498 F.3d 1345 (Fed. Cir. 2007). Until the Examiner has established a *prima facie* case of obviousness, the Applicants need not present arguments or evidence of non-obviousness. To establish a *prima facie* case of obviousness, the Examiner must establish at least three elements. First, the prior art references when combined must teach or suggest all of the claim limitations: "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 165 U.S.P.Q. 494, 496 (CCPA 1970); *see also M.P.E.P. § 2143.03*. Second, there must be a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091 (Fed. Cir. 1986); *see also M.P.E.P. § 2143.02*. And finally, the Examiner must articulate some reason to modify or combine the cited references that renders the claim obvious. *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1740-1741 (2007).

Applicants respectfully assert that a *prima facie* obviousness has not been established because the cited references, in combination with the knowledge of one of skill in the art, do not teach or suggest all of the claim limitations. Furthermore, the combined teachings of the cited art fail to provide any reasonable expectation of success of arriving at the claimed invention.

Claims 19-21 and 30

Dependent Claims 19-21 and 30 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Linnecke in view of Singh *et al.* (U.S. Patent Publication No. 20020034827). Linnecke describes an agglutination assay using latex beads. Singh *et al.* discloses general methods and materials for the extraction and analysis of complex materials. *See* Singh *et al.*, Abstract.

As discussed above, independent Claim 18, from which Claims 19-21 and 30 depend, has been amended to relate to colloidal particles that comprise a lipid layer. The amendment to Claim 18 renders the rejections of dependent Claims 19-21 and 30 moot because the combination of Linnecke and Singh *et al.* fails to teach colloidal particles comprising a lipid layer.

Claims 22-24, 28, and 31

Dependent Claims 22-24, 28, and 31 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Linnecke in view of Schaertl *et al.* (*J Biomol Screen* 2000; 5(4):227-237) (hereinafter "Schaertl"). Schaertl discloses the labeling of nanoparticles for immunoassays. *See* Schaertl *et al.*, Abstract.

As discussed above, the features of canceled Claim 22 has been incorporated into amended Claim 18 to reflect that the colloidal particles comprise a lipid layer. Claim 28 recites colloidal particles coated with a lipid layer, while Claims 23 and 31 recite a natural cell membrane. Claim 24 recites covalent linking between the ligand and colloidal particle.

Although Linnecke does not disclose a lipid layer, the Examiner asserts that the nanoparticle of Schaertl inherently includes a lipid layer and could be used to increase the range of analytes for detection in Linnecke. *Final Office Action of April 5, 2010*, page 5. However, Schaertl does not, in fact, teach a nanoparticle that inherently includes a lipid layer or a lipid layer that could be used with Linnecke's latex beads with any reasonable expectation of success.

Applicant previously explained why Schaertl does not teach a colloidal particle comprising a lipid layer and further does not teach a lipid layer that can be combined with the latex beads of Linnecke with any reasonable expectation of success. However, the Examiner did not address these arguments in the Advisory Action of July 28, 2010. Applicants respectfully request the Examiner to duly consider the following discussion of Linnecke and Schaertl.

The Examiner argues that "one of the species of nanoparticles used was non-replicating E. coli" (page 5, 1st pp). However, no reasonable interpretation of the term "nanoparticle" would include a bacterial cell, such as that described by Schaertl. Schaertl does not teach a colloidal particle comprising a lipid layer, but rather discloses artificial nanoparticles on one hand, and whole bacteria on the other hand. Moreover, Schaertl explicitly teaches that the artificial nanoparticles are *completely distinct* from the whole bacteria used in the described fluorescence immunoassay. Emphasizing the difference between the nanoparticles and bacteria, Schaertl states, "The use of a bacterial display system instead of nanoparticles enables the expression of protein A derivative directly on the cell surface, so that antibodies can be linked." *Schaertl* at page 228, column 1 (emphasis added). Furthermore, Schaertl concludes, "The bacteria can fulfill the function of a bead-like carrier...it is not relevant if the bacteria are live or dead as long as their structural integrity is preserved" *Id.* at page 228, column 2 (emphasis added). Thus, Schaertl is unequivocal that nanoparticles and whole bacteria are entirely different structures. As such, a person of ordinary skill in the art would comprehend that Schaertl does not teach a *colloidal particle comprising a lipid layer*.

Moreover, Schaertl teaches away from combination with the latex beads of Linnecke and the colloidal particles of instant claims by explicitly stating that the structural integrity of the bacteria must be preserved. *Id.* Much less providing any reasonable expectation of success, Schaertl unambiguously discourages a person of ordinary skill in the art from disrupting the structural integrity of the bacteria and somehow adapting its lipid layer onto the latex beads of Linnecke, as apparently alleged by the Examiner. Furthermore, even if there were a way to combine the bacteria with the latex beads of Linnecke without disrupting the integrity of bacteria, there is no reason to do so.

In the claimed system, the lipid layer is used to maintain the colloidal particles near the claimed phase transition state. Furthermore, the lipid layer allows a wide variety of analytes to

be measured including analytes that bind to ligands associated with a lipid layer. However, a person of ordinary skill would have no reason to combine the whole bacteria of Schaertl with the latex beads of Linnecke because it would be unclear whether a hypothetical bacterium-latex bead structure could even be used in an agglutination assay. One of ordinary skill in the art would likely believe that such a lipid layer would interfere with binding of the bead-bound antigen to the antibody being analyzed, as opposed to being any kind of improvement in such an assay. Indeed, the bacteria in Schaertl are used in a fluorescence based detection assay, suggesting that a person of ordinary skill would not be able to use the bacteria with any reasonable expectation of success in the Linnecke agglutination assay, which is analyzed spectroscopically by light transmission.

As such, Linnecke fails to teach or suggest all of the claim limitations of amended Claim 18 and Claims 22, 24, 28, and 31 in view of Schaertl. Moreover, there is also no reason to make the claimed combination because Schaertl teaches away from disrupting the structural integrity of the bacteria and one of ordinary skill in the art would not believe that such a combination would have a reasonable chance of success to operate for its intended purpose.

Claim 26

Claim 26, which depends from amended Claim 18, has been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Linnecke.

As discussed above, Claim 18 has been amended to be drawn to colloidal particles comprising a lipid layer. Because Linnecke does not teach a lipid layer, Linnecke fails to disclose each and every limitation of the claim and therefore fails to establish a *prima facie* case of obviousness with respect to Claim 26, which includes the limitations of amended Claim 18.

Claim 29

Dependent Claim 29 has been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Linnecke in view of Faulds *et al.* (*Analyst* 2002; 127:282-86). Faulds *et al.* discloses the use of a microscope to detect light scattering of gold or silver colloid surfaces. Faulds *et al.*, Abstract.

Claim 29 recites detection using a microscope.

As discussed above, Linnecke, in combination with the knowledge of one of skill in the art, does not teach or suggest all of the claim limitations and further fails to provide any reasonable expectation of success for arriving at Claim 28 or the claims depending therefrom (including Claim 29). As such, the combination of Linnecke and Faulds fails to establish a *prima facie* case of obviousness with respect to Claim 29.

Claims 33-35, and 37

Dependent Claims 33-35 and 37 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Linnecke in view of Strauss (US 4410660). Strauss discloses silica or metal particles.

Claims 33-35 and 37 are drawn to colloidal particles comprising a lipid layer or coated with a lipid layer. Neither Linnecke nor Strauss teaches a lipid layer. As such, the combination of Linnecke and Strauss fails to establish a *prima facie* case of obviousness with respect to Claims 33-35 and 37, which depend from Claim 18 or 28 and characterize the single central particle.

Based on the foregoing, Linnecke, in combination with the knowledge of one of skill in the art and the cited references, does ***not*** teach or suggest all of the claim limitations but in fact teaches away from them, nor would it have been obvious to modify the assay of Linnecke to arrive at the claimed methods. Applicants therefore respectfully request withdrawal of the rejections under 35 U.S.C. § 103(a).

CONCLUSION

Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. In light of the above amendments and remarks concerning the pending claims, Applicants respectfully request allowance of the pending claims. If the Examiner has any questions which may be answered by telephone, the Examiner is invited to call the undersigned directly.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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